

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2002 Budget Request

Witness appearing before the
House Subcommittee on Labor-HHS-Education Appropriations

Dr. Judith L. Vaitukaitis, Director
National Center for Research Resources

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Statement by

Dr. Judith L. Vaitukaitis
Director, National Center for Research Resources
National Institutes of Health

on

Fiscal Year 2002 President's Budget Request
for the National Center for Research Resources

Mr. Chairman and Members of the Committee:

I am pleased to present the President's budget request for the National Center for Research Resources (NCRR) for Fiscal Year 2002, a sum of \$974,038,000, which reflects an increase of \$156,785,000 over the Fiscal Year 2001 appropriation.

It is a pleasure once again to have the opportunity to present the accomplishments of NCRR-supported research and future directions for NCRR programs. With the human genome and several others essentially sequenced, biomedical research is entering a new age. Up until now, biomedical science has benefitted greatly from a reductionist perspective which examines single genes or their encoded macromolecules to determine the cause of disease. But today, new research technologies enable scientists to pry ever deeper into the cell to uncover the structural and functional secrets of the ribosome which serves as the cell's protein factory and also to find hundreds of disease-associated proteins. With advanced technologies investigators have discovered defective membrane potassium channels responsible for some forms of epilepsy or abnormal heart rhythms that may be fatal if the genetic abnormalities resulting in altered potassium channel function are not detected and treated.

Sophisticated biomedical research now frequently requires a multidisciplinary approach with teams that include physician-investigators, physicists, bioinformaticists, physical chemists, structural biologists, and others. The research team must not only take full advantage of existing novel research tools but must also develop novel ones to solve new complex research problems.

To facilitate this new paradigm for research, NCRR's programs need to modify or generate new, more sophisticated resources to enable research in the 21st century. NCRR provides the critical research infrastructure that enables all lines of biomedical inquiry, from the molecular level to the whole organism. Specially adapted clinical research facilities assure that the fruits of bench research reach the patient. The network of NCRR's General Clinical Research Centers (GCRCs) require sophisticated core laboratories and bioinformatics tools to facilitate research. To foster multisite research collaborations, NCRR supports development of web-based research networks for clinical trials and research on the molecular and other causes of disease.

To enhance access to costly technologies, NCRR works in partnership with other Federal agencies, such as the Department of Energy and the National Science Foundation (NSF). For decades, NCRR has funded a substantial research effort to improve x-ray crystallography techniques. NCRR has been a pivotal player in developing very high intensity x-ray sources for biological research at the national synchrotron facilities, through cooperative approaches with DOE and NSF staff. The nation's synchrotron facilities are critical for ascertaining the structures of biological molecules encoded by thousands of genes. With the incorporation of robotics, newer imaging technologies along with methods to automate data collection and processing, an appropriately equipped research resource may conduct more than one hundred thousand crystallization experiments per day! Using NCRR research resources, studies in the past required years of effort, will be accomplished in a week!

NCRR also supports programs to enhance the research capabilities of minority-serving graduate institutions through the Research Centers in Minority Institutions (RCMI) program. Separately, through the Institutional Development Award (IDeA) program, NCRR provides funding for capacity building for biomedical research in those states which have not previously participated fully in the research programs of the NIH. The current cohort of 23 IDeA-eligible states and Puerto Rico receives about five percent of NIH grant funds annually.

GENOMICS AND GENETIC MEDICINE

To determine the genetic causes of diseases, large numbers of patients must be screened for specific gene variants. NCRR proposes to support national genotyping laboratories to provide a cost-effective, high throughput approach. Genotyping attempts to find nucleotide substitutions at specific points, or loci, within a gene that may be defective and cause disease. In addition, NCRR proposes to expand the capacities of its mouse mutant regional resource centers network to accommodate a rapidly expanding pool of mouse mutants and to support a web-based catalog of their genetic variants and physical characteristics or phenotype. The mutant mouse network's catalog will facilitate investigator access to mouse mutants needed for their research.

Scientists today urgently need improved or new technologies to study the thousands of proteins that interact with one another to make a cell function as a tightly controlled unit. This complex research requires an integrated or systems approach. In response, NCRR proposes to develop and support comprehensive Integrated Biomedical Technology Resource Centers, where multiple complementary technologies examine the inner workings of both healthy and diseased cells. Research areas that can be facilitated through integrative approaches include those for proteomics, imaging, structural biology and glycobiology.

NCRR proposes to develop the rhesus macaque as a nonhuman primate model of genetic disease in humans. In collaboration with the National Human Genome Research Institute, NCRR will provide support for the development of BAC (Bacterial Artificial Chromosome) libraries as well as for genetic and radiation hybrid maps. New

technologies have made it theoretically possible to selectively modify genes of nonhuman primates to create defects that mimic human diseases, such as cystic fibrosis. Studies will also address how risk factors modulate gene function in polygenic disorders such as type 2 diabetes mellitus and hypertension.

BIOENGINEERING, BIOIMAGING, AND BIOINFORMATICS

Today's biomedical research depends on sophisticated research technologies more so than in the past. NCRR proposes to increase support for instruments in the \$100,000 to \$500,000 range through its Shared Instrumentation Grant (SIG) Program. The off-the-shelf instruments in greatest demand through the SIG program include confocal microscopes, NMR spectrometers, cell sorters, mass spectrometers and protein/DNA sequencers. To address the broad research community needs of the instrumentation that costs between \$500,000 and several million dollars, NCRR proposes to initiate a new program to provide advanced instrumentation that includes very-high-field NMR spectrometers, synchrotron facilities, mass spectrometers, cryoelectron microscopes, and high-performance supercomputers.

To further enhance the national infrastructure for biomedical research, NCRR will establish a biomedical imaging research network (BIRN) test bed for development of hardware, software, and protocols to effectively share and mine data in a site-independent manner for both basic and clinical research. For this undertaking, NCRR has teamed up with the San Diego Supercomputer Center, one of three National Science Foundation-supported centers for advanced computational infrastructure, to provide biomedical investigators access to sophisticated modeling and computational tools. Other partners include the NSF, University of California at San Diego and several NIH Institutes along with seven institutions with NCRR-supported general clinical research centers, co-located with imaging technology centers. The BIRN will include image data with high-bandwidth requirements, as well as genomic, structural, and gene expression data. The BIRN will be designed so that it can be readily expanded to meet the evolving needs of basic and clinical investigators across a network of resource centers that provide access to specialized research facilities, repositories and regional core facilities to enable research nationwide.

NEW PREVENTIVE STRATEGIES AGAINST DISEASE

Not all research advances lie in medical genetics. Scientists have observed recently that transplantation of insulin-producing human pancreas cells, called islet cells, to patients with type I diabetes can free them from the need for insulin injections. But to get a sufficient supply of these scarce and difficult-to-isolate cells, cell-harvesting efficiency and islet cell stability need to be optimized. To pursue these very promising results, which eventually may provide a cure for type I diabetes, NCRR—together with the National Institute of Diabetes and Digestive and Kidney Diseases and the Juvenile Diabetes Research Foundation International—will establish several Islet Cell Resource Centers to optimize the isolation, purification, and function of islet cells for transplantation into patients with type I diabetes.

As clinical research becomes more complex and promising new therapies are evaluated, more attention to the safety of research subjects must be taken. The NCRR will provide support for a Research Subject Ombudsman (RSO) at each General Clinical

Research Center (GCRC) and RCMI Clinical Research Center to ensure that the research subject monitoring plan at these resources is fully implemented and carried out according to the Institutional Review Board-approved protocol. The Ombudsman will also ensure that investigators report serious adverse events within a required time frame to appropriate agencies, offices or Boards. The RSO will also keep patients and volunteers informed about the research projects and clinical trials in which they participate.

HEALTH DISPARITIES

To address the health concerns of minority populations, NCCR proposes to establish Comprehensive Centers for Health Disparities Research at minority-serving medical schools associated with the NCCR-funded Research Centers in Minorities Institutions. These Centers will further develop their medical schools' capacities to conduct basic and clinical research on type II diabetes and cardiovascular disease, which disproportionately affect minority populations. The Centers will support further development of the host institution's research infrastructure, including laboratories, faculty recruitment of established clinical investigators and development of promising junior faculty. Collaboration with nearby research-intensive universities will be strongly encouraged. To further strengthen these minority institutions, NCCR also proposes to establish a Web-based clinical trials network for minority-serving institutions. This new network will better position minority-serving medical schools to more fully participate in NIH-supported research, including multi-site clinical trials that address diseases that disproportionately affect minorities and underserved populations.

RESEARCH TRAINING AND CAREER DEVELOPMENT

Proper training in research methodology is essential for young scientists. NCCR proposes to initiate new mentored programs for medical and veterinary students to develop their research skills and pique their interests in research careers to enhance the pool of well-trained young physicians and veterinarians who will become the independent investigators for tomorrow's health-related research.

In addition to expanding support for the Mentored Patient-Oriented Research Career Development Award (K23), NCCR proposes to initiate a new career development program for physicians and dentists through a mentored institutional Clinical Research Scholars (CRS) program. That CRS pilot program will be phased in over several years at approximately ten institutions. The flexible program will provide tuition support for didactic courses, leading to an M.S., Ph.D. or M.P.H. degree. The CRS program support for candidate development of clinical and bench patient-oriented research skills in a mentored setting is central to this new program. The long term CRS program goal is to enhance the pool of high quality independent clinical investigators.

RESEARCH CAPACITY

Adequate, up-to-date facilities are indispensable for biomedical research. The greater biocomplexity of modern research requires state-of-the-art research facilities. Through the NIH Research Facilities Improvement Program, NCCR will expand its support to help address this need.

Modern research facilities are also needed to provide care and housing for chimpanzees that were originally bred for AIDS research. So far, chimpanzees have not proven to be suitable models for studies of AIDS pathogenesis, but they are essential for studies of respiratory syncytial virus, hepatitis, malaria, and possibly for AIDS vaccine and gene vector development. To consolidate the NIH-supported chimps into just two or three sites, animal housing must be constructed to provide cost-effective facilities that will assure the well-being and safety of the animals and people who work with them. Funding to construct a chimpanzee sanctuary system is also needed to accommodate chimpanzees no longer eligible or required for research.

NCRR proposes to increase the level of support for the Animal Facilities Improvement Program. About half of all NIH research grants include animal research models and institutions need to build specially adapted, modern research facilities to accommodate these genetically altered rodents. A special initiative to upgrade the research animal facilities of minority graduate and health profession schools will be continued to help those institutions meet PHS standards and receive accreditation by the Association for Assessment and Accreditation of Laboratory Animal Care (International).

Through the Biomedical Research Infrastructure Network (BRIN), the NIH's Institutional Development Award program enhances the educational infrastructure and research capacities of institutions within 23 eligible states and Puerto Rico. The BRINs provide support for laboratory renovation and scientific equipment, as well as the recruitment and support of faculty at eligible institutions. In Fiscal Year 2002, NCRR proposes to further develop the BRINs that were initially established in Fiscal Year 2001. In addition, those states that did not receive a BRIN award in Fiscal Year 2001 will have a special opportunity to compete for this award in Fiscal Year 2002.

The NIH budget request includes the performance information required by the Government Performance and Results Act (GPRA) of 1993. Prominent in the performance data is NIH's second annual performance report which compared our FY 2000 results to the goals in our FY 2000 performance plan. As performance trends on research outcomes emerge, the GPRA data will help NIH to identify strategies and objectives to continuously improve its programs.

My colleagues and I will be happy to respond to any questions you may have.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

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BIRTHPLACE: Hartford, Connecticut

EDUCATION: B.S., Tufts University, 1962
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EXPERIENCE:

Following house staff training in internal medicine at Bellevue Hospital (Cornell), the Memorial-Sloan Kettering Hospital in New York City and University Hospital in Boston (1966-69), Dr. Vaitukaitis completed postdoctoral training in reproductive endocrinology at Boston University School of Medicine and at the National Institute of Child Health and Human Development. She also served as a Senior Investigator in the National Institute of Child Health and Human Development's intramural program in Bethesda. She returned to Boston in 1974 as an Associate Professor of Medicine at Boston University School of Medicine where she conducted basic and clinical research studies in reproductive endocrinology. She served as Professor of Medicine at Boston University School of Medicine (1977-86). She also directed Boston University's General Clinical Research Center (1977-86) and headed the Section on Endocrinology and Metabolism at Boston City Hospital (1974-86).

In 1993, Dr. Vaitukaitis became the Director of the National Center for Research Resources. Prior to that she served as Director of NCRR's General Clinical Research Centers Program, a position she initially assumed in July 1986, and subsequently became NCRR's Deputy Director in 1991.

She has published over 160 scientific papers in both basic and clinical research and has had four publications selected as Citation Classics. She is Editor of one book, Clinical Reproductive Neuroendocrinology. She has served on numerous editorial boards of scientific journals and has served on many advisory boards and committees for the National Institutes of Health, other Federal agencies, universities, private foundations as well as scholarly societies. She is an elected member of the American Society for Clinical Investigation, Association of American Physicians, The Endocrine Society and the Institute of Medicine of the National Academy of Sciences.